CAGCGTCAGACGCAGGGCACTGAGAATGTGCGACAGCGCGCAACGATGAAGTAGCCCAGAGGGTCCCTTG
GAAAATGAGGCCAGGGTCCCTGCTGCTGCTTGTTCTGCTGCTCGCCCTGTCCAGGAGCCTGCGGGGCAAA
GAGTGTGCGTCTCCACCCTGTGAGTGTCACCAGGAGGACGACTTCAGAGTCACCTGCAAGGAGCTCCACC
GAATCCCCAGCCTGCCGCCCAGCACCCAGACTCTGAAGCTCATCGAGACTCATCTGAAGACCATACCCAG
TCTTGCATTTTCGAGTCTGCCCAATATTTCCAGGATCTATTTATCTATAGATGCAACTCTGCAGCGGCTG
GAACCACATTCTTTCTACAATTTGAGTAAAATGACTCACATAGAAATCCGGAACACCAGAAGCTTAACCT
ATATAGACCCTGATGCCTTGACAGAGCTCCCCTTGCTCAAGTTTCTTGGCATTTTCAATACTGGACTTAG
AATATTCCCTGACTTGACCAAAATTTATTCCACGGACATATTCTTTATACTTGAAATCACAGACAACCCT
TACATGACTTCGGTCCCTGAAAACGCATTCCAGGGCCTATGCAATGAAACCTTGACCCTGAAACTGTACA
ACAATGGATTTACTTCAGTCCAAGGACATGCTTTCAATGGAACAAAGCTGGATGCTGTTTACCTAAACAA
GAATAAATACCTGACAGCTATAGACAACGATGCCTTTGGAGGAGTATACAGTGGACCAACTTTGCTAGAT
GTGTCTTCCACCAGCGTCACTGCCCTTCCTTCCAAAGGCCTGGAGCACCTCAAAGAACTGATCGCAAAAG
ACACCTGGACTCTCAAAAAGCTCCCGCTGTCGTTGAGTTTCCTCCACCTCACTCGGGCTGACCTCTCTTA
CCCGAGCCACTGCTGCGCTTTTAAGAACCAGAAGAAAATCAGGGGAATCCTGGAGTCTTTGATGTGTAAT
GAGAGCAGTATCCGGAACCTTCGTCAAAGGAAATCAGTGAACATCTTGAGGGGTCCCATCTACCAGGAAT
ATGAAGAAGATCCGGGTGACAACAGTGTTGGGTACAAACAAAACTCCAAGTTCCAGGAGAGCCCAAGCAA
CTCTCACTATTACGTCTTCTTTGAAGAACAAGAGGATGAGGTCGTTGGTTTCGGCCAAGAGCTCAAAAAT
CCTCAGGAAGAGACTCTCCAAGCCTTCGAGAGCCACTATGACTACACGGTGTGTGGGGACAACGAGGACA
TGGTGTGTACCCCCAAGTCGGACGAGTTTAACCCCTGTGAAGATATCATGGGCTACAGGTTCCTGAGAAT
CGTGGTGTGGTTTGTCAGTCTGCTGGCTCTCCTGGGCAATATCTTCGTCCTGCTCATTCTGCTAACCAGC
CACTACAAATTGACCGTGCCGCGGTTCCTCATGTGCAACTTGGCCTTTGCAGATTTCTGCATGGGGGTAT
ACCTGCTTCTCATTGCCTCTGTAGACCTGTACACACACTCTGAGTACTACAACCACGCCATCGACTGGCA
GACGGGCCCTGGGTGCAACACGGCTGGCTTCTTCACTGTTTTCGCCAGTGAGTTATCAGTGTACACACTG
ACGGTCATCACCCTGGAGCGATGGTACGCCATCACCTTCGCCATGCGCCTGGATAGGAAGATCCGCCTCA
GGCACGCGTACACCATCATGGCTGGGGGCTGGGTTTCCTGCTTCCTTCTCGCCCTGCTCCCGATGGTGGG
AATCAGCAGCTATGCCAAGGTCAGCATCTGCCTGCCAATGGACACCGACACCCCTCTTGCACTCGCATAC
ATTGTCCTCGTTCTGCTGCTCAATGTTGTTGCCTTTGTTGTCGTCTGTTCCTGCTATGTGAAGATCTACA
TCACGGTCCGAAATCCCCAGTACAACCCTCGAGATAAAGACACCAAGATTGCCAAGAGGATGGCTGTGTT
GATCTTCACTGACTTCATGTGCATGGCGCCCATCTCCTTCTATGCGCTGTCGGCACTTATGAACAAGCCT
CTAATCACTGTTACTAACTCCAAAATCTTGTTGGTTCTCTTCTACCCCCTCAACTCCTGTGCCAATCCGT
TTCTCTATGCTATTTTCACCAAGGCCTTCCAGAGGGACGTGTTCATCCTGCTCAGCAAGTTTGGCATCTG
CAAACGCCAGGCCCAGGCCTATCAGGGTCAGAGAGTCTGTCCCAACAATAGCACTGGTATTCAGATCCAA
AAGATTCCCCAGGACACGAGGCAGAGTCTCCCCAACATGCAAGATACCTATGAACTGCTTGGAAACTCCC
AGCTAGCTCCAAAACTGCAGGGACAAATCTCAGAAGAGTATAAGCAAACAGCCTTGTAAAGGAAAGGCTA
CGCTAGTCACAGTGAGACTTACAAAAGGCTGGTTTCTTGAACATGCGTTCCAGTCCCGTGACATGTGAAC
ACATAGGTTCATGCAGGTGATGATTCATAGGGTCAGAGTTCATCTCTAGAAAGTATTGCCTC
(SEQ ID NO:1)

FIGURE 1A

MRPGSLLLLVLLLALSRSLRGKECASPPCECHQEDDFRVTCKELHRIPSLPPSTQTLKLIETHLKTIPSLAFSSLPN
ISRIYLSIDATLQRLEPHSFYNLSKMTHIEIRNTRSLTYIDPDALTELPLLKFLGIFNTGLRIFPDLTKIYSTDIFF
ILEITDNPYMTSVPENAFQGLCNETLTLKLYNNGFTSVQGHAFNGTKLDAVYLNKNKYLTAIDNDAFGGVYSGPTLL
DVSSTSVTALPSKGLEHLKELIAKDTWTLKKLPLSLSFLHLTRADLSYPSHCCAFKNQKKIRGILESLMCNESSIRN
LRQRKSVNILRGPIYQEYEEDPGDNSVGYKQNSKFQESPSNSHYYVFFEEQEDEVVGFGQELKNPQEETLQAFESHY
DYTVCGDNEDMVCTPKSDEFNPCEDIMGYRFLRIVVWFVSLLALLGNIFVLLILLTSHYKLTVPRFLMCNLAFADFC
MGVYLLLIASVDLYTHSEYYNHAIDWQTGPGCNTAGFFTVFASELSVYTLTVITLERWYAITFAMRLDRKIRLRHAY
TIMAGGWVSCFLLALLPMVGISSYAKVSICLPMDTDTPLALAYIVLVLLLNVVAFVVVCSCYVKIYITVRNPQYNPR
DKDTKIAKRMAVLIFTDFMCMAPISFYALSALMNKPLITVTNSKILLVLFYPLNSCANPFLYAIFTKAFQRDVFILL
SKFGICKRQAQAYQGQRVCPNNSTGIQIQKIPQDTRQSLPNMQDTYELLGNSQLAPKLQGQISEEYKQTAL
(SEQ ID NO:2)

FIGURE 1B

underlined = deleted in targeting construct

[ ] = sequence flanking Neo insert in targeting construct

[CAGCGTCAGACGCAGGGCACTGAGAATGTGCGACAGCGCGCAACGATGAAGTAGCCCAG
AGGGTCCCTTGGAAAATGAGGCCAGGGTCCC] TGCTGCTGCTTGTTCTGCTGCTCGCCCT
GTCCAGGAGCCTGCGGGGCAAAGAGTGTGCGTCTCCACCCTGTGA [GTGTCACCAGGAGG
ACGACTTCAGAGTCACCTGCAAGGAGCTCCACCGAATCCCCAGCCTGCCGCCCAGCACCC
AGACTCT] GAAGCTCATCGAGACTCATCTGAAGACCATACCCAGTCTTGCATTTTCGAGT
CTGCCCAATATTTCCAGGATCTATTTATCTATAGATGCAACTCTGCAGCGGCTGGAACCA
CATTCTTTCTACAATTTGAGTAAAATGACTCACATAGAAATCCGGAACACCAGAAGCTTA
ACCTATATAGACCCTGATGCCTTGACAGAGCTCCCCTTGCTCAAGTTTCTTGGCATTTTC
AATACTGGACTTAGAATATTCCCTGACTTGACCAAAATTTATTCCACGGACATATTCTTT
ATACTTGAAATCACAGACAACCCTTACATGACTTCGGTCCCTGAAAACGCATTCCAGGGC
CTATGCAATGAAACCTTGACCCTGAAACTGTACAACAATGGATTTACTTCAGTCCAAGGA
CATGCTTTCAATGGAACAAAGCTGGATGCTGTTTACCTAAACAAGAATAAATACCTGACA
GCTATAGACAACGATGCCTTTGGAGGAGTATACAGTGGACCAACTTTGCTAGATGTGTCT
TCCACCAGCGTCACTGCCCTTCCTTCCAAAGGCCTGGAGCACCTCAAAGAACTGATCGCA
AAAGACACCTGGACTCTCAAAAAGCTCCCGCTGTCGTTGAGTTTCCTCCACCTCACTCGG
GCTGACCTCTCTTACCCGAGCCACTGCTGCGCTTTTAAGAACCAGAAGAAAATCAGGGGA
ATCCTGGAGTCTTTGATGTGTAATGAGAGCAGTATCCGGAACCTTCGTCAAAGGAAATCA
GTGAACATCTTGAGGGGTCCCATCTACCAGGAATATGAAGAAGATCCGGGTGACAACAGT
GTTGGGTACAAACAAAACTCCAAGTTCCAGGAGAGCCCAAGCAACTCTCACTATTACGTC
TTCTTTGAAGAACAAGAGGATGAGGTCGTTGGTTTCGGCCAAGAGCTCAAAAATCCTCAG
GAAGAGACTCTCCAAGCCTTCGAGAGCCACTATGACTACACGGTGTGTGGGGACAACGAG
GACATGGTGTGTACCCCCAAGTCGGACGAGTTTAACCCCTGTGAAGATATCATGGGCTAC
AGGTTCCTGAGAATCGTGGTGTGGTTTGTCAGTCTGCTGGCTCTCCTGGGCAATATCTTC
GTCCTGCTCATTCTGCTAACCAGCCACTACAAATTGACCGTGCCGCGGTTCCTCATGTGC
AACTTGGCCTTTGCAGATTTCTGCATGGGGGTATACCTGCTTCTCATTGCCTCTGTAGAC
CTGTACACACACTCTGAGTACTACAACCACGCCATCGACTGGCAGACGGGCCCTGGGTGC
AACACGGCTGGCTTCTTCACTGTTTTCGCCAGTGAGTTATCAGTGTACACACTGACGGTC
ATCACCCTGGAGCGATGGTACGCCATCACCTTCGCCATGCGCCTGGATAGGAAGATCCGC
CTCAGGCACGCGTACACCATCATGGCTGGGGGCTGGGTTTCCTGCTTCCTTCTCGCCCTG
CTCCCGATGGTGGGAATCAGCAGCTATGCCAAGGTCAGCATCTGCCTGCCAATGGACACC
GACACCCCTCTTGCACTCGCATACATTGTCCTCGTTCTGCTGCTCAATGTTGTTGCCTTT
GTTGTCGTCTGTTCCTGCTATGTGAAGATCTACATCACGGTCCGAAATCCCCAGTACAAC
CCTCGAGATAAAGACACCAAGATTGCCAAGAGGATGGCTGTGTTGATCTTCACTGACTTC
ATGTGCATGGCGCCCATCTCCTTCTATGCGCTGTCGGCACTTATGAACAAGCCTCTAATC
ACTGTTACTAACTCCAAAATCTTGTTGGTTCTCTTCTACCCCCTCAACTCCTGTGCCAAT
CCGTTTCTCTATGCTATTTTCACCAAGGCCTTCCAGAGGGACGTGTTCATCCTGCTCAGC
AAGTTTGGCATCTGCAAACGCCAGGCCCAGGCCTATCAGGGTCAGAGAGTCTGTCCCAAC
AATAGCACTGGTATTCAGATCCAAAAGATTCCCCAGGACACGAGGCAGAGTCTCCCCAAC
ATGCAAGATACCTATGAACTGCTTGGAAACTCCCAGCTAGCTCCAAAACTGCAGGGACAA
ATCTCAGAAGAGTATAAGCAAACAGCCTTGTAAAGGAAAGGCTACGCTAGTCACAGTGAG
ACTTACAAAAGGCTGGTTTCTTGAACATGCGTTCCAGTCCCGTGACATGTGAACACATAG
GTTCATGCAGGTGATGATTCATAGGGTCAGAGTTCATCTCTAGAAAGTATTGCCTC

FIGURE 2A

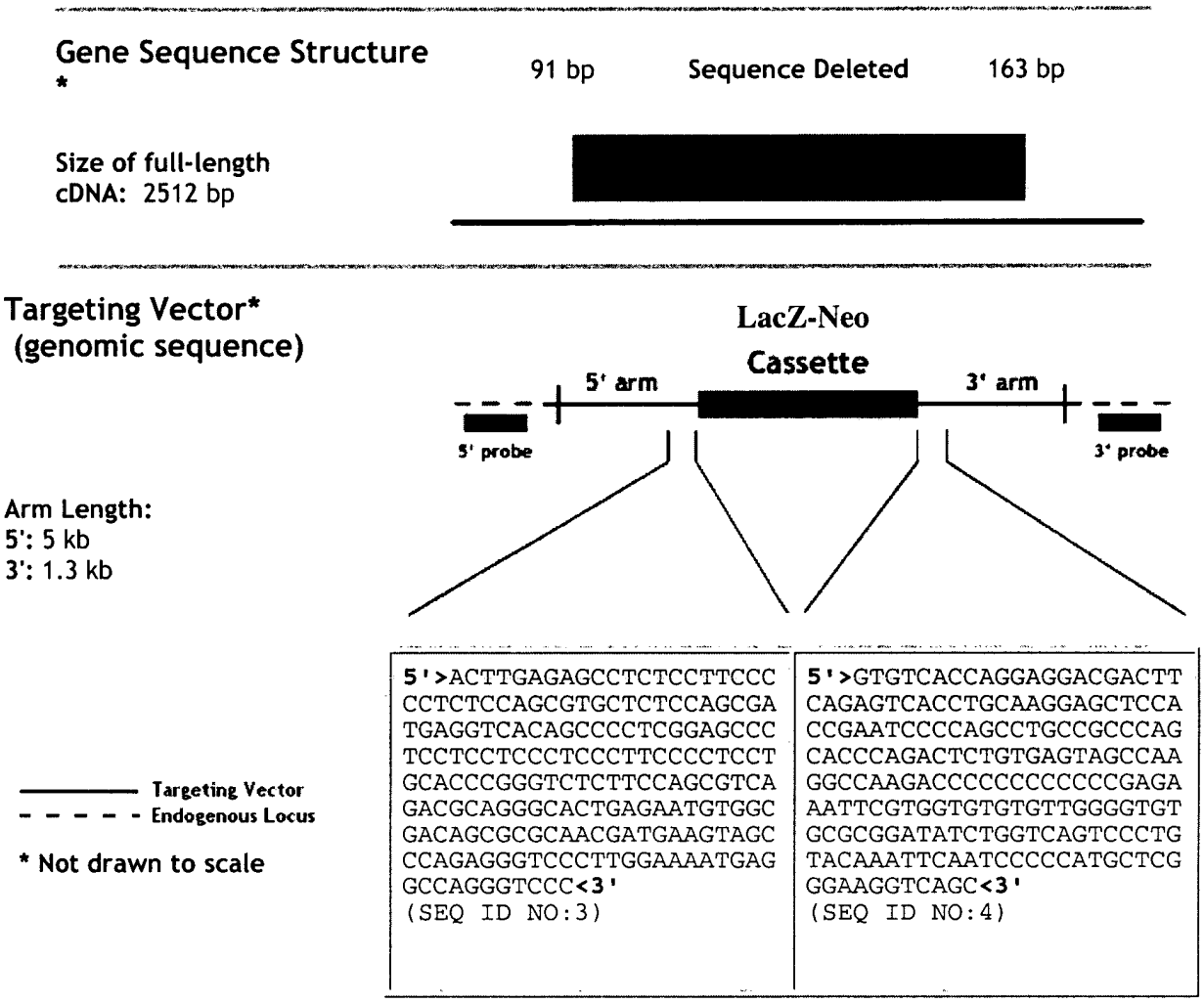
Gene Sequence Structure
*
91 bp
Sequence Deleted
163 bp
Size of full-length
cDNA: 2512 bp
Targeting Vector*
(genomic sequence)
LacZ-Neo
Cassette
5' arm
3' arm
5' probe
3' probe
Arm Length:
5': 5 kb
3': 1.3 kb
Targeting Vector
Endogenous Locus
* Not drawn to scale
5'>ACTTGAGAGCCTCTCCTTCCC
CCTCTCCAGCGTGCTCTCCAGCGA
TGAGGTCACAGCCCCTCGGAGCCC
TCCTCCTCCCTCCCTTCCCCTCCT
GCACCCGGGTCTCTTCCAGCGTCA
GACGCAGGGCACTGAGAATGTGGC
GACAGCGCGCAACGATGAAGTAGC
CCAGAGGGTCCCTTGGAAAATGAG
GCCAGGGTCCC<3'
(SEQ ID NO:3)
5'>GTGTCACCAGGAGGACGACTT
CAGAGTCACCTGCAAGGAGCTCCA
CCGAATCCCCAGCCTGCCGCCCAG
CACCCAGACTCTGTGAGTAGCCAA
GGCCAAGACCCCCCCCCCCCGAGA
AATTCGTGGTGTGTGTTGGGGTGT
GCGCGGATATCTGGTCAGTCCCTG
TACAAATTCAATCCCCCATGCTCG
GGAAGGTCAGC<3'
(SEQ ID NO:4)

FIGURE 2B

	Gender	Age (days)	Length (cm)	Body Weight (g)	Spleen Weight (g)	Spleen/ Body Weight (%)	Liver Weight (g)	Liver/ Body Weight (%)	Kidney Weight (g)	Kidney/ Body Weight (%)	Thymus Weight (g)	Thymus/ Body Weight (%)	Heart Weight (g)	Heart/ Body Weight (%)	Testes + Epididymis Weight (g)
+/+	Female	48	10	22.339	0.095	0.425	1.256	5.622	0.327	1.464	0.082	0.367	0.155	0.694	
+/+	Female	48	8.25	16.960	0.052	0.307	0.900	5.307	0.220	1.297	0.060	0.354	0.122	0.719	
+/+	Male	48	9.5	24.550	0.069	0.281	1.388	5.654	0.342	1.393	0.055	0.224	0.119	0.485	0.224
+/+	Male	48	9.7	23.792	0.081	0.340	1.192	5.010	0.304	1.278	0.063	0.265	0.133	0.559	0.226
-/+	Female	48	8.5	22.619	0.080	0.354	1.272	5.624	0.238	1.052	0.080	0.354	0.121	0.535	
-/+	Male	48	9	24.040	0.072	0.300	1.344	5.591	0.322	1.339	0.062	0.258	0.137	0.570	0.181
-/-	Female	47	7.5	9.026	0.008	0.089	0.435	4.819	0.110	1.219	0.010	0.111	0.045	0.499	
-/-	Female	48	7	8.360	0.016	0.191	0.382	4.569	0.110	1.316	0.004	0.048	0.051	0.610	
-/-	Female	48	8	11.640	0.016	0.137	0.586	5.034	0.127	1.091	0.031	0.266	0.053	0.455	
-/-	Male	48	7.6	11.733	0.018	0.153	0.666	5.676	0.134	1.142	0.034	0.290	0.053	0.452	0.087
-/-	Male	48	8	12.545	0.024	0.191	0.778	6.202	0.146	1.164	0.035	0.279	0.060	0.478	0.180
-/-	Male	48	7	8.070	0.007	0.087	0.366	4.535	0.095	1.177	0.001	0.012	0.042	0.520	0.076

FIGURE 3

	Gender	Age at Test (days)	Length (cm)	Body Weight (g)	Spleen Weight (g)	Spleen/ Body Weight (%)	Liver Weight (g)	Liver/ Body Weight (%)	Kidney Weight (g)	Kidney/ Body Weight (%)	Thymus Weight (g)	Thymus/ Body Weight (%)	Heart Weight (g)	Heart/ Body Weight (%)	Testes + Epididymis Weight (g)
+/+	Female	308	9.5	25.191	0.222	0.8813	1.476	5.8592	0.353	1.4013	0.039	0.1548	0.145	0.5756	
+/+	Female	308	9.918	28.180	0.091	0.3229	1.447	5.1348	0.383	1.3591	0.043	0.1526	0.136	0.4826	
+/+	Male	308	11.025	55.089	0.182	0.3304	3.267	5.9304	0.694	1.2598	0.074	0.1343	0.219	0.3975	0.35
+/+	Male	308	11	42.613	0.136	0.3192	2.144	5.0313	0.485	1.1382	0.052	0.1220	0.201	0.4717	0.387
-/-	Female	307	7.978	19.561	0.030	0.1534	0.863	4.4118	0.184	0.9406	0.040	0.2045	0.109	0.5572	
-/-	Male	307	9.47	25.557	0.077	0.3013	1.394	5.4545	0.340	1.3304	0.025	0.0978	0.111	0.4343	0.401
-/-	Male	307	9.5	25.263	0.051	0.2019	1.232	4.8767	0.296	1.1717	0.027	0.1069	0.102	0.4038	0.389

FIGURE 4